

Constipation and catharsis

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Constipation is endemic in the Western world. Stool consistence and associated symptoms are more important than stool frequency. The patient's attitude towards his bowel habit is also important. Exclusion of "organic" disease, reassurance and discussion of normal variations of bowel habit are necessary first steps in treatment. Adequate bulk in the stool must be ensured, either through diet or bulking agents, and bowel retraining attempted. Laxatives should be reserved for episodes of constipation following enforced bedrest, or as a preparation for diagnostic procedures. Long-term use should be avoided.

La constipation est endémique dans le monde occidental. La consistance des selles et les symptômes associés sont plus importants que la fréquence de la défécation. L'attitude du patient à l'égard de ses habitudes de défécation est aussi importante. Après avoir éliminé la possibilité d'une cause organique, les premières étapes nécessaires au traitement consistent à rassurer le patient et à discuter avec lui des variations normales des habitudes de défécation. On doit assurer un volume de selles adéquat, par le régime alimentaire ou à l'aide d'agents mucilagineux, et une rééducation des habitudes de défécation doit être tentée. Les laxatifs doivent être réservés aux épisodes de constipation tels ceux qui suivent les périodes d'alitement forcées, ou à la préparation pour les tests de diagnostic. Leur utilisation en traitement prolongé doit être évitée.

Of the beliefs handed down to us by our forefathers, the concept of regularity is among the most enduring. Since antiquity an empty colon has been equated with purity; and what generations of mothers have cherished, let no man put asunder. Nevertheless, there is a logical approach to "constipated" patients, and physicians should be firm in their convictions, which, in turn, should be based on science, not fantasy.

The definition of constipation is elusive. The world's record for rectal continence is held by a man who resisted the temptations of the toilet for 368 days.¹ He is said to have become weak after delivering 36 l of feces on June 21, 1901, but "there was much rejoicing in the family". Statistically the "normal population" has from three bowel movements per week to three a day.² The 1% of individuals who fall outside that range are unusual but not necessarily abnormal. It is probable that the actual frequency of motions is not relevant, although it may be of great concern to the patient. More important are the consistence of the stool and associated symptoms.

Pathophysiologic considerations

There are two modes of colonic motor activity.³ The first is propulsive contractions or mass movements, long recognized by radiologists. These peristaltic rushes are more frequent in diarrhea than in constipation. The other mode is segmental or nonpropulsive activity, which appears to have a mixing and braking function. Such activity tends to be decreased in diarrhea and increased in some patients with constipation. Segmentation that succeeds in isolating part of the colon from the remainder may generate very high pressures and result in proximal dilatation or diverticula formation.

In the spastic type of irritable colon syndrome the stool is hard, scybalous and often associated with lower abdominal pain.⁴ These symptoms relate to excessive segmental contraction of the lower colon and rectum, and the individual subsequently has a feeling of incomplete evacuation. Constipation may alternate with periods of diarrhea. Hemorrhoids and fissures may complicate the passage of stony stools. Less commonly, obstipation may result from an atonic, lax colon, in which progressive peristaltic activity is decreased, a condition characterized by Sir Arthur Hurst as dyschezia.⁵ This may occur spontaneously but is also seen following chronic abuse of laxatives.

Constipation may result from a wide variety of local and systemic conditions. Perianal disorders such as fissures or localized proctitis may lead to conscious or subconscious defence of the area by the withholding of stool. Cancer of the colon, diverticular disease and volvulus are causes of a recent change in bowel habit and must be rigorously excluded. In hypothyroidism or dehydration, appropriate replacement therapy may be curative. Many drugs, including codeine, some antihypertensive agents, iron, aluminum and calcium compounds, are constipating. Inactivity, such as that following surgery, or travel, especially with change in time zones, may induce this distressing nuisance, and it is a frequent consequence of pregnancy and of old age. Endogenous depression often produces constipation, which may improve with antidepressant therapy. Parents reward their children for a successful bowel action and imbue in many the idea that daily movements are essential for cleanliness or purity. Psychoanalysts have attributed repression of defecation to anal eroticism. If the patient is an unmarried girl it is said that marriage may effect a cure.⁶

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I know of no controlled trials to substantiate this.

Constipation, like the irritable colon, diverticular disease and appendicitis, is a disease of Western civilization, apparently attributable to our low-fibre, refined diet.⁷ It has been demonstrated that the daily stool weight in English subjects is one third that of Africans living under native conditions on an unrefined diet.⁸ The transit time of the bulky African stool is less than half that of the British. It would appear that our colons have not had time to adapt to the fibre-free, low-bulk stool that has resulted from the refined diet adopted over the past century. Thus, partially filled colons can generate very high segmental pressures, accounting for the pain and constipation of the spastic colon. Peristaltic activity is disordered and the patient may have an increased transit time. In individuals who are given 20 g of unprocessed bran daily, the stool bulk is significantly increased by water entrapped in the interstices of the dietary residue.⁹ Such treatment speeds up transit in those in whom it was slow and, paradoxically, slows transit in those in whom it was rapid. In other words, increased dietary bulk normalizes colon motility.^{9,10} Coarse bran is more effective than fine because of the former's greater water-holding capacity.¹¹

The individual with constipation may complain of foul breath, furred tongue, anorexia, flatulence, headache, irritability, insomnia, and so on. These were once considered manifestations of auto-intoxication.¹² Proponents of this concept held that poisons were elaborated in the gut as a result of constipation. In one experiment, however, five healthy men were required to eat normally but refrain from defecation for 90 hours.¹³ Each man complained of the above symptoms and experienced immediate relief when the situation was reversed by an enema. Such prompt relief seems to militate against toxemia, and the symptoms are now believed to be due to distension and mechanical irritation of the rectum. In fact, masses of cotton wool packed into the rectum produce identical effects.^{12,13} Many individuals whose colons may be empty may incorrectly blame such common symptoms on constipation, and on this basis indulge in excessive purgation.

There is no doubt that constipation is distressful. Empires have trembled at the prospect of doing without purgatives. In an exercise of pharmacologic warfare Britain placed an embargo on the export of purgatives to Napoleon-controlled Europe.¹⁴ This strategy was expounded by one Sydney Smith:

What a sublime thought that no purge

can now be taken between the Weser and the Garonne; that the bustling pestle is still, the canorous mortar mute, and the bowels of men locked up for fourteen degrees of latitude . . . Without castor oil they might for some months, to be sure, have carried on a lingering war; but what can they do without bark [cascara]?¹⁴

Investigation

Organic disease must be excluded. This demands careful history-taking and physical examination and, at least, sigmoidoscopy.¹⁵ Most patients should have a barium enema examination and an estimation of hemoglobin concentration. Recent onset of constipation demands rigorous exclusion of local and systemic disease, particularly carcinoma of the colon, hypothyroidism and depression. The patient's drug history should be carefully reviewed to ensure that there is not a pharmacologic cause for his symptoms.

Treatment

General measures

It is believed by many that exercise promotes a normal bowel habit. Conversely, enforced confinement to bed, such as after a coronary occlusion or a fractured hip, is frequently associated with constipation, especially if the patient must grapple with pulleys and bedpans. Adequate fluid must also be ensured. The chronically constipated colon may be retrained. This is best achieved by using natural reflexes to advantage. It is recognized that the resting colon may be spurred into action by a meal, particularly breakfast. Many individuals insist that their bowels function only following their customary morning coffee or cigarette, although whether this effect is pharmacologic, physiologic or psychologic is uncertain. The regular post-breakfast retirement with a good book to the relaxing solitude of the bathroom may have a salutary effect. It is said that a low toilet seat results in a squatting position, which is more favourable for defecation. Certainly a draughty outhouse in January is no place to commence the exercise. To initiate the habit in those accustomed to taking laxatives it may be necessary to use an enema for the first while. A glycerine suppository, while inactive pharmacologically, may set in motion the defecation reflex. Patient attention to such details, along with the use of bulking agents as described below, may restore even the most recalcitrant colon to normalcy.

Bulking agents

Dietary fibre is described as "unavailable carbohydrate" and includes cel-

lulose, hemicellulose and lignin.¹⁶ In addition to its hydrophilic bulking properties fibre may have a cathartic effect due to the volatile fatty acids released by bacterial metabolism. Since there is much evidence that deficiency of fibre or bulk is an important factor in constipation, it seems reasonable to increase the intake of fibre by constipated patients.¹⁷ As Cleave⁷ forcefully states, this means less refined sugar and flour, and more natural fruits and whole-wheat products. Bran has long been recognized as an effective laxative and this has had scientific confirmation.^{9,10,18,19} Miller's bran, 6 to 10 teaspoonfuls (12 to 20 g) per day, is a cheap and effective laxative.^{9,10,16,18} Coarse bran has been shown to have a greater water-holding capacity than bran made finer by milling;¹¹ this accounts for the greater effectiveness of the former in improving transit time. The resourceful patient may improve palatability of this material by adding it to cereals, sauces, meat loaves and other foods. Liberal use of whole-wheat bread, breakfast cereals and fresh fruits and vegetables may assist in providing extra bulk.

Since bran in therapeutic quantities is inconvenient, many physicians now prescribe bulking agents. The most satisfactory of these is psyllium hydrophilic mucilloid (Metamucil, Hydrocil). This is useful for preventing constipation and other manifestations of the irritable colon syndrome, as an adjunct to the therapy of perianal disease, and in the prevention, not the treatment, of acute diverticulitis. It is superior to methylcellulose for this purpose.²⁰ The appeal of the use of bulking agents is their almost complete lack of side effects, although impaction is a potential hazard if they are given to patients with underlying obstructing lesions.²¹ Metamucil contains dextrose as a dispersing agent and is best taken in juice, 1 to 3 teaspoonfuls three times a day with meals. Some patients have transient bloating with the commencement of therapy, but the dose may be adjusted to achieve a stool that is formed — neither loose and watery, nor stony and fragmented. For patients who are fussy there is an expensive flavoured preparation.

To understand better how psyllium exerts its effect, one can perform the following simple experiment. In a medicine glass place 5 ml of the psyllium powder. Add water to make up a total of 30 ml. Stir and allow to stand for a few minutes. You will notice that a soft gel forms in the glass. In the colon this gelling action may soften a hard, marble-like stool or firm a watery one. The added bulk promotes normal peristalsis.

Anticholinergics

Anticholinergic drugs have a greater action on the segmenting or braking contractions of the colon than on peristalsis.²² Thus, they may be of use in treating colonic spasm when it manifests itself as abdominal pain.²³ Anticholinergics achieve an effect on the colon only in doses that cause side effects such as tachycardia and dry mouth. Further, they may aggravate colonic stasis and lead to drying of the stool.²⁴ Dicyclomine hydrochloride (Bentylol) is said to have a specific effect on smooth muscle with less effect on secretion.²⁵ If this were true it would be the best antispasmodic to use. Otherwise, synthetic agents offer no practical advantages over atropine, are expensive and are poorly absorbed from the gut. It is therefore a sad comment that atropine preparations to be taken orally are not available in Canada. Anticholinergics have very little applicability in constipation and should be tried only in cases in which abdominal pain presumably due to colonic segmental spasm is not controlled by bulking agents. Patients who have postprandial pain due to an exaggerated "gastrocolic" reflex may occasionally benefit from the administration of an effective dose before meals.

Stool softeners

Stool softeners are used to lubricate the stool and are often recommended by surgeons for perianal disease. There are many reasons why mineral oil (liquid paraffin) should not be used. Aspiration (lipoid) pneumonia has been reported in the elderly^{26,27} and in infants.²⁸ Mineral oil is a solvent for the fat-soluble vitamins A, D, E and K, and thus may interfere with their absorption.^{29,30} If used in patients with enteric fistulas it may interfere with healing.³¹ Further, if used excessively it may actually cause incontinence, and oil leaking through the anal sphincter may cause pruritis ani.³² Mineral oil has even been blamed for gastrointestinal cancer. For these reasons mineral oil should be banished from the market place.

Diocetyl sodium sulfosuccinate (DSS) is an anionic detergent, which, by lowering surface tension, is thought to facilitate penetration of the fecal mass by water and fat.³² Like mineral oil it produces its laxative effect by softening the stool, apparently through inhibition of water absorption.³⁴ This substance should be reserved for those situations in which a stool softener is required for a short period — that is, acute perianal disease. DSS may facilitate the absorption of other normally unabsorbed laxa-

tives and should not be used in drug combinations.³⁵

Chemical stimulants

Chemical stimulant laxatives can be used in relative safety provided they are not abused. The diphenylmethane laxative phenolphthalein, originally intended as a wine colouring, is present in many patent medicines. Some of the dye is absorbed and appears in the urine, which, if alkaline, may become pink or red.³⁶ It may undergo enterohepatic circulation. The absorbed drug is believed to act directly on the muscle of the distal colon to stimulate peristalsis.³⁷ It acts within 6 to 8 hours after ingestion and is not inhibited by atropine. The usual dose is 200 mg. Even in 200 times the usual dose it is remarkably nontoxic, although hypersensitivity reactions have been reported.³⁸ Long-term use and abuse, on the other hand, may have devastating effects (see below). Oxyphenisatin, a relative of phenolphthalein, has been associated with the development of chronic active hepatitis.^{35,39-41} The responsible preparation contained DSS, which may have facilitated the absorption of oxyphenisatin and its transport to the liver.³⁵ Bisacodyl (Dulcolax) is the most useful of this series of drugs and can be given either as a suppository or by mouth. The enteric-coated tablet has no action on the small bowel. If, however, the tablets are taken orally with an alkali, the coating may dissolve, allowing the drug to act on the small bowel, causing unpleasant gastrointestinal symptoms. Bisacodyl does not work for 6 hours or more following oral administration. It is therefore ideally given the night before the desired morning evacuation. The suppository will have more prompt action, reflexly stimulating the whole colon.⁴² The stimulant effect of the diphenylmethane cathartics is inhibited by local anesthesia.⁴³

The anthracene glycosides include senna and cascara and are more potent than phenolphthalein.⁴⁴ The mechanism of the catharsis effected by these orally administered drugs is due to direct action on the submucosal nerve plexus in the colon; the effect is blocked by prior application of local anesthetic.⁴⁵ Senna is the active principle of liquorice powder. The intact glycoside is ineffective in the colon.^{45,46} When administered orally it is apparently hydrolyzed by colonic bacteria to release aglycones, which cause peristalsis of the transverse and descending colon and decrease sigmoid segmentation,⁴⁷ a process that requires 6 to 8 hours. Aglycones are ineffective when administered orally.⁴⁵ Long-term use leads to a peculiar pigmentation of the rectal mucosa called melanosis coli.⁴⁸

Abuse of diphenylmethane and anthracene cathartics has been associated with a number of serious complications. Long-term use results in dependence of the bowel on these drugs for "successful" function. In mice and in one woman subjected to long-term administration of senna, damaged myenteric neurons were demonstrated in the colon.⁴⁸ Thus, the patient may become physiologically and psychologically dependent on continued purgation. A frequent result is, paradoxically, diarrhea.⁴⁹⁻⁵² For reasons best known to themselves such patients may conceal their laxative habit from the hapless physician who is dutifully investigating their copious diarrhea. A radiograph of the colon may show loss of haustrations and smooth, tapering contractions known as pseudostrictures.⁴⁹ In one such patient finger clubbing developed, which delayed recognition of purgative abuse.⁵³ The clubbing disappeared when the senna was withdrawn, only to reappear when purgative abuse was resumed. In these misguided patients the diagnosis of laxative abuse may only be confirmed by "locker search" or examination of the urine for phenolphthalein or anthraquinone derivatives.^{50,51,53} A further clue to laxative abuse may be an associated hypokalemia,^{51,54,55} which may resemble hyperaldosteronism.⁵⁶ Malabsorption and protein-losing enteropathy have also been described.^{50,52}

Saline cathartics

The saline cathartics consist of a variety of magnesium and sodium salts. Their effect depends in part upon their ionization, osmotic effect and low absorbability. There is also good evidence that magnesium and sulfate ions in the gut cause secretion of cholecystokinin.⁵⁷ This hormone in turn stimulates intestinal and colonic motility. Magnesium sulfate (Epsom salt) is a commonly used saline cathartic. It has a bitter, unpleasant taste but causes a semifluid evacuation in less than 3 hours when given in a dose of 5 to 15 g.⁴³ It is therefore useful to rid the gut of blood in patients with hepatic coma, of drugs in poisoning situations and of worms after administration of a vermifuge. Milk of magnesia (magnesium hydroxide), more often used as an antacid, is also a saline cathartic but has a relatively mild action. Magnesium-containing salts should be given with caution to patients with impaired renal function. Sodium-based compounds may be taken orally, but the most commonly used sodium-containing saline cathartic, sodium phosphate-biphosphate compound (Fleet), is available as an enema. This hyperosmolar solution is available in small plastic

containers. It is sometimes described as a "disposable enema", although one is unlikely to encounter an enema that anyone would wish to keep. This preparation is most useful in fecal or barium impaction and in preparing the rectum for sigmoidoscopy. A hypertonic or any other type of enema may cause mucosal irritation, which interferes with interpretation of sigmoidoscopic findings.⁵⁸ Therefore, it is better to attempt the examination first and at least get a look at the mucosa. One can administer an enema subsequently if necessary.

Miscellaneous

Castor oil, a triglyceride expressed from the seeds of a tropical African plant, has been used as a cathartic for 3500 years. It is hydrolyzed in the small intestine by pancreatic enzymes to release glycerol and ricinoleic acid;⁴³ the latter produces hypermotility of the small and large bowel. Castor oil produces abdominal cramping and loose bowel motions within 2 hours and if used in excess may induce electrolyte imbalance. Because of this violent action it is unsuitable for routine use and should be reserved for situations in which total colonic cleanout is necessary, such as for a barium enema or colonoscopy.

Lactulose is a synthetic disaccharide not digested by small intestinal or pancreatic enzymes. In the colon it is metabolized by the microflora, with resultant acidification of the stool and re-

lease of gas. It is effective in treating constipation and changes the nature of the colon flora.⁵⁹ The main indication is portal-systemic encephalopathy because it decreases the availability of ammonia and other amines from the gastrointestinal tract to the brain.⁶⁰ The drug is too costly for routine purgation and with long-term use there is risk of superinfection.⁶¹

There are other traditional laxatives that are now considered obsolete. These include mercury-containing compounds such as calomel, and mucosal irritants such as croton oil. The latter has been used to alter the political views of prisoners and would seem to have limited appeal in a democracy.⁶² Podophyllum, a resin used to remove warts, is no longer considered a practical cathartic. Oral bile salts have a direct stimulating effect on the colon and, in addition, inhibit the absorption of salt and water.⁶³ The resultant catharsis explains the durability of that ancient preparation still on druggists' shelves, Caroid and Bile Salts. Because of the adverse effects of bile salts in the stomach and the existence of many other effective agents, this preparation can no longer be considered useful.⁶⁴

Conclusion

Constipation, like beauty, "often lies in the eyes of the beholder". It is a sobering thought that many patients purge themselves because they think they are constipated.²⁴ In one study, 14 of 20 patients using laxatives habitually for constipation were able to maintain a satisfactory bowel habit during a 2-week period on a placebo.⁶⁵ Thus, the physician must first determine that the patient is indeed constipated. Laxatives should be reserved for episodes of constipation such as may occur after barium radiography or enforced bedrest. The types of laxatives available and the time lags in their action are summarized in Table I.

In a lecture delivered nearly 40 years ago Witts⁶⁶ urged his colleagues to refrain from ritual purgation of their patients. He pointed out that purging "any unfortunate patient who is robust enough to stand the strain" pre- and postoperatively is a practice "rooted in archaic and primitive beliefs, rather than physiology and pathology." Seriously ill patients in a state of precarious hydration can ill afford further gastrointestinal loss of fluid. In spite of injunctions by clinical pharmacologists against their long-term use, over 700 laxative preparations are available over the counter in the United States,¹⁷ and these are dispensed literally by the ton.⁶⁷ Like King Lear in the storm, the physician must stand firm on his scien-

tific convictions and defy this costly and harmful tide.

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References

1. GEIB D, JONES JD: Unprecedented case of constipation. *JAMA* 38: 1305, 1902
2. CONNELL AM, HILTON C, IRVINE G, et al: Variation of bowel habit in two population samples. *Br Med J* 2: 1095, 1965
3. MISIEWICZ JJ: Colonic motility. *Gut* 16: 311, 1975
4. THOMPSON WG: The irritable colon. *Can Med Assoc J* 111: 1236, 1974
5. HURST AF: *Constipation and Allied Intestinal Disorders*, London, Oxford U Pr, 1919
6. TRUELOVE SC, REYNELL PC: *Diseases of the Digestive System*, 2nd ed, Oxford, Blackwell, 1972, p 389
7. CLEAVE TL: *The Saccharine Disease*, Bristol, Wright, 1974
8. BURKITT DP, WALKER ARP, PAINTER NS: Effect of dietary fibre on stools and transit time and its role in the causation of disease. *Lancet* 2: 1408, 1972
9. HEATON KW, PAYLER D, POMARE EW, et al: The relationship between intestinal transit time and stool weight, and the effects of bran (abstr). *Gastroenterology* 66: 843, 1974
10. LYFORD C, FISHER J, BUSS B, et al: Controlled clinical trial of bran in irritable bowel syndrome (abstr). *Clin Res* 23: 247, 1975
11. KIRWAN WO, SMITH AN, MCCONNELL AA, et al: Action of different bran preparations on colonic function. *Br Med J* 4: 187, 1975
12. ALVAREZ WC: Intestinal autointoxication. *Physiol Rev* 4: 352, 1924
13. DONALDSON AN: Relation of constipation to intestinal intoxication. *JAMA* 78: 884, 1922
14. SMITH S: cited in In England Now. *Lancet* 2: 1079, 1973
15. THOMPSON WG: Sigmoidoscopy. *Can Med Assoc J* 110: 683, 1974
16. CUMMINGS JH: Progress report: dietary fibre. *Gut* 14: 69, 1973
17. LAXATIVES and dietary fiber. *Med Lett Drugs Ther* 15: 98, 1973
18. PAINTER NS: Aetiology of diverticular disease. *Br Med J* 2: 156, 1971
19. COWGILL GR, ANDERSON WE: Laxative effects of wheat bran and "washed bran" in healthy men. *JAMA* 98: 1866, 1932
20. CASS LJ, WOLF LP: A clinical evaluation of certain bulk and irritant laxatives. *Gastroenterology* 20: 149, 1952
21. SOUTER WA: Bolus obstruction of gut after use of hydrophilic colloid laxatives. *Br Med J* 1: 166, 1965
22. PAINTER NS, TRUELOVE SC, ANDRAN GM, et al: Effect of morphine, prostigmine, pethidine and Pro-Banthine on the human colon in diverticulosis studied by intra-luminal pressure recorders and cineradiology. *Gut* 6: 57, 1965
23. IVEY KJ: Are anticholinergics of use in the irritable colon syndrome? *Gastroenterology* 68: 1300, 1975
24. INGELFINGER FJ: The treatment of chronic constipation. *Ann NY Acad Sci* 58: 503, 1954
25. GOODMAN LS, GILMAN A: *The Pharmacological Basis of Therapeutics*, 4th ed, New York, Macmillan, 1970, p 540
26. ZURROW HB, SERGAY H: Lipoid pneumonia in a geriatric patient. *J Am Geriatr Assoc* 14: 240, 1966
27. FREIMAN DG, ENGELBERG H, MERRIT WH: Oil aspiration (lipoid) pneumonia in adults: a study of 47 patients. *Arch Intern Med* 66: 11, 1940
28. ELSTON CW: Pneumonia due to liquid paraffin: a chemical analysis. *Arch Dis Child* 41: 428, 1966
29. Effect of mineral oil on the absorption of carotene and vitamin A in man (E). *Nutr Rev* 6: 170, 1948
30. JAVERT CT, MACRI C: Prothrombin concentration and mineral oil. *Am J Obstet Gynecol* 42: 409, 1941
31. DONALD I: *Practical Obstetrical Problems*, 3rd ed, London, Lloyd Lake, 1964, p 743
32. JONES A, GODDING EW: *Management of Constipation*, Oxford, Blackwell, 1972, chap 2, part 2, p 38
33. BOYD JT, DOLL R: Gastro-intestinal cancer and the use of liquid paraffin. *Br J Cancer* 8: 231, 1954

Table I—Types of laxatives available and time lags in their action

Type		Time lag
Bulking agents	Bran	Days
	Psyllium Methylcellulose	
Stool softeners	Mineral oil*	Days
	Diocetyl sodium sulfosuccinate	
Chemical stimulants	Diphenylmethane Phenolphthalein Oxyphenisatin* Bisacodyl	6 hours
	Anthracene glycosides Senna Cascara	
Saline cathartics	Magnesium sulfate Magnesium hydroxide Sodium sulfate	3 hours
Miscellaneous	Castor oil Lactulose Calomel* Croton oil* Podophyllum* Caroid and Bile Salts*	— 2 hours

*Obsolete.

34. SAUNDERS DR, SILLERY J, RACHMILEWITZ D: Effect of dioctyl sodium sulfosuccinate (DSS) on structure and function of human and rat intestine (abstr). *Gastroenterology* 68: 979, 1975
35. NAESS K: Oxyphenisatin and jaundice. *JAMA* 212: 1961, 1970
36. FANTUS B, DYNIEWICZ JM: Phenolphthalein studies. Elimination of phenolphthalein. *JAMA* 110: 1656, 1938
37. BLICK P, BERARDI JB, WOZASEK O: The mode of the laxative action of phenolphthalein. *Am J Dig Dis* 9: 292, 1942
38. ABRAMOWITZ EW: Phenolphthalein today: a critical review. *Am J Dig Dis* 17: 79, 1950
39. REYNOLDS TD, LAPIN AC, PETERS RL, et al: Puzzling jaundice: probable relationship to laxative ingestion. *JAMA* 211: 86, 1970
40. MACHARDY G, BALART LA: Jaundice and oxyphenisatin. *Ibid*, p 83
41. PEARSON AJG, GRAINGER JM, SCHAUER DJ, et al: Jaundice due to oxyphenisatin. *Lancet* 1: 994, 1971
42. KOCK NG, KEWENTER J, SUNDIN T: Studies on the defecation reflex in man. *Scand J Gastroenterol* 7: 689, 1972
43. GOODMAN LS, GILMAN A: *Pharmacological Basis of Therapeutics*, op cit, p 1020
44. HUBACHER MH, DOERNBERG S: Laxatives. II. Relationship between structure and potency. *J Pharm Sci* 53: 1067, 1964
45. HARDCASTLE JD, WILKINS JL: The action of sennosides and related compounds on human colon and rectum. *Gut* 11: 1038, 1970
46. SMITH B: Effect of irritant purgatives on the myenteric plexus in man and the mouse. *Gut* 9: 139, 1968
47. WALLER S: Comparative effects of codeine and senna on the motor activity of the left colon (abstr). *Gut* 16: 407, 1975
48. BOCKUS HL, WILLARD JH, BANK J: Melanosis coli: the etiological significance of the anthracine laxatives. A report of 41 cases. *JAMA* 111: 1, 1933
49. RAWSON MD: Cathartic colon. *Lancet* 1: 1121, 1966
50. FRENCH JM, GADDIE R, SMITH N: Diarrhoea due to phenolphthalein. *Lancet* 1: 551, 1956
51. CUMMINGS JH, SLADEN GE, JAMES OFW, et al: Laxative-induced diarrhoea: a continuing clinical problem. *Br Med J* 1: 537, 1974
52. HEIZER WD, WARSHAW AL, WALDMANN TA, et al: Protein-losing gastroenteropathy and malabsorption associated with factitious diarrhoea. *Ann Intern Med* 68: 839, 1968
53. SILK DDA, GIBSON JA, MURRAY CRH: Reversible finger clubbing in a case of purgative abuse. *Gastroenterology* 68: 790, 1975
54. SCHWARTZ WB, RELMAN AS: Metabolic and renal studies in chronic potassium depletion resulting from overuse of laxatives. *J Clin Invest* 32: 258, 1953
55. HOUGHTON BJ, PEARS MA: Chronic potassium depletion due to purgation with cascara. *Br Med J* 1: 1328, 1958
56. FLEISCHER N, BROWN H, GRAHAM DY, et al: Chronic laxative induced hyperaldosteronism and hypokalemia simulating Bartter's syndrome. *Ann Intern Med* 70: 791, 1969
57. HARVEY RF, READ AE: Saline purgatives act by releasing cholecystokinin. *Lancet* 2: 185, 1973
58. DEVROEDE G, LERICHE M, SANCHEZ G, et al: Effects of hypertonic enemas on the rectal mucosa (abstr). *Ann R Coll Phys Surg Can* 8: 27, 1975
59. WESSELIUS-DE CASPARIS A, BRAADBAART S, BERGH-BOHLKEN GE, et al: Treatment of chronic constipation with lactulose syrup: results of a double blind study. *Gut* 9: 87, 1968
60. ELKINGTON SG: Lactulose. *Gut* 11: 1043, 1970
61. DUBOS RJ, SAVAGE DC, SCHAEDELER RW: The indigenous flora of the gastrointestinal tract. *Dis Colon Rectum* 10: 23, 1967
62. GADDUM JH: *Pharmacology*, 4th ed, London, Oxford U Pr, 1953, p 251
63. MEKJIAN HS, PHILLIPS SF, HOFFMAN AF: Colonic secretion of water and electrolytes induced by bile acids: perfusion studies in man. *J Clin Invest* 50: 1569, 1971
64. HEATON KW: The importance of keeping bile salts in their place. *Gut* 10: 857, 1969
65. GREINER T, BROSS I, GOLD H: A method for evaluation of laxative habits in human subjects. *J Chronic Dis* 6: 244, 1957
66. WITTS LJ: Ritual purgation in modern medicine. *Lancet* 1: 427, 1937
67. TRAVELL J: Pharmacology of stimulant laxatives. *Ann NY Acad Sci* 58: 416, 1954

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Rx summary

Indications

The following types of infections when caused by susceptible pathogens:

- Genitourinary tract infections: acute, recurrent, and chronic cystitis, pyelonephritis, urethritis (including uncomplicated gonococcal urethritis), prostatitis, vaginitis, cervicitis, salpingitis
- Upper and lower respiratory tract infections (particularly chronic bronchitis and including acute and chronic otitis media)
- Gastrointestinal tract infections

It is not indicated in infections due to *Pseudomonas*, *Mycoplasma*, or viruses.

Contraindications

Evidence of marked liver damage; blood dyscrasias; known hypersensitivity to trimethoprim or sulfonamides; or marked renal impairment where repeated serum assays cannot be carried out.

Infants during the first few weeks of life (especially premature infants).

For the time being, during pregnancy.

Adverse reactions

Most frequent: nausea; vomiting; gastric intolerance; and rash.

Less frequent: diarrhea; constipation; flatulence; anorexia; pyrosis; gastritis; gastroenteritis; urticaria; headache; and liver changes (abnormal elevations in alkaline phosphatase and serum transaminase). Occasionally reported: glossitis; oliguria; hematuria; tremor; vertigo; alopecia; and elevated BUN, NPN, and serum creatinine.

Hematological changes, occurring particularly in the elderly, are mostly transient and reversible (primarily, neutropenia and thrombocytopenia; less frequently, leukopenia, aplastic or hemolytic anemia, agranulocytosis, and bone marrow depression).

Precautions

As with other sulfonamide preparations, benefit should be critically appraised against risk in patients with liver damage, renal damage, urinary obstruction, blood dyscrasias, allergies, or bronchial asthma.

The possibility of superinfection with a non-sensitive organism should be borne in mind.

Dosage and administration

Children under 12 years of age:

Young children - according to weight

Under 2 years - 2.5 ml suspension, twice daily

2 to 5 years - 2.5 to 5 ml suspension or 1 to 2 pediatric tablets, twice daily

6 to 12 years - 5 to 10 ml suspension or 2 to 4 pediatric tablets or 1 adult tablet, twice daily

Adults and children over 12 years of age:

Standard dosage - 2 adult tablets, twice daily

Minimum dosage and long-term treatment - 1 adult tablet, twice daily

Maximum dosage (overwhelming infections) - 3 adult tablets, twice daily

Uncomplicated gonorrhea - 2 adult tablets, 4 times daily for 2 days

For acute urinary tract infections, 2 tablets twice daily should be given until the urine becomes sterile.

When the patient has a history of chronic reinfection, 1 tablet twice daily can be given as prophylaxis.

Supply

Suspension (anisced-flavoured), each teaspoonful (5 ml) containing 40 mg trimethoprim plus 200 mg sulfamethoxazole. Bottles of 100 and 400 ml.


Pediatric tablets, containing 20 mg trimethoprim plus 100 mg sulfamethoxazole. Bottles of 100 and 500.

Adult tablets, containing 80 mg trimethoprim plus 400 mg sulfamethoxazole. Bottles of 100 and 500.

Product monograph available on request.

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 Hoffmann-La Roche Limited
Vaudreuil, Quebec

Dalmane[®] Roche[®] (flurazepam)

Rx summary:

Indications Useful in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening. 'Dalmane' can be administered effectively for short-term and intermittent use in patients with recurring insomnia and poor sleeping habits; however, the safety and efficacy of long-term use has not been established.

Contraindications Known hypersensitivity to the drug and, because of lack of sufficient clinical experience, in children under fifteen years of age.

Warnings Safety in women who are or may become pregnant has not been established; hence as with all medication, 'Dalmane' should be given only when the potential benefits have been weighed against possible hazard to mother and child.

Precautions *Use in the Elderly:* In elderly and debilitated patients, it is recommended that the dosage initially be limited to 15 mg to preclude the development of oversedation, dizziness and/or ataxia reported in some patients.

Use in Emotional Disorders: The usual precautions are indicated for severely depressed patients or those in whom there is any evidence of latent depression, particularly the recognition that suicidal tendencies may be present and protective measures may be necessary.

Potential of Drug Effects: Since 'Dalmane' has a central nervous system depressant effect, patients should be advised against the simultaneous ingestion of alcohol and other central nervous system depressant drugs during 'Dalmane' therapy.

Physical and Psychological Dependence: As with any hypnotic, caution must be exercised in administering to individuals known to be addiction-prone or those whose history suggests they may increase the dosage on their own initiative.

General: All patients should be cautioned against engaging in activities requiring precision and complete mental alertness such as in operating machinery or driving a motor vehicle shortly after ingesting the drug. Should 'Dalmane' be used repeatedly, periodic blood counts and liver and kidney function tests should be performed. The usual precautions should be observed in patients with impaired renal or hepatic function. Patients' reactions will be modified to a varying extent depending on dosage and individual susceptibility.

Adverse Effects Dizziness, drowsiness, lightheadedness and ataxia may occur. These adverse effects are particularly common in elderly and debilitated patients. (See Precautions).

Severe sedation, lethargy, disorientation, probably indicative of drug intolerance or overdose, have been reported.

Dosage Dosage should be individualized for maximal beneficial effects. The usual adult dosage is 30 mg before retiring. In elderly and/or debilitated patients, it is recommended that therapy be initiated with 15 mg until individual responses are determined. Moderate to severe insomnia may require 15 or 30 mg.

Supply 'Dalmane' 15, capsules (orange and ivory) 15 mg, 100 and 500.

'Dalmane' 30, capsules (red and ivory) 30 mg, 100 and 500.

Complete prescribing information available on request.

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 Hoffmann-La Roche Limited
Vaudreuil, Québec